



Modeling and Simulation Framework for Value-based Healthcare Systems

Journal:	<i>Simulation: Transactions of the Society for Modeling and Simulation International</i>
Manuscript ID	S-17-0230.R1
Manuscript Type:	3 Special Issue
Date Submitted by the Author:	n/a
Complete List of Authors:	Traoré, Mamadou; LIMOS CNRS UMR 6158, Université Blaise Pascal Zacharewicz, Gregory; University Bordeaux 1, Laboratory IMS-LAPS CNRS Team Productique (GRAI); Duboz, Raphaël; CIRAD, ES-AGIR Zeigler, Bernie; university of arizona, ECE;
Key Words and Phrases:	Theory and Methodology -> DEVS Methodology , Applications in Management - Planning and Forecasting -> General , Applications in Science and Engineering -> Biomedical and Medicine
Abstract:	Regardless of the coordination of its activities, a healthcare system is composed of a large number of distributed components that are interrelated by complex processes. Understanding the behavior of the overall system is becoming a major concern among healthcare managers and decision makers. This paper presents a modeling and simulation framework to support a holistic analysis of healthcare systems through a stratification of the levels of abstraction into multiple perspectives and their integration in a common simulation framework. In each of the perspectives, models of different components of healthcare system can be developed and coupled together. Concerns from other perspectives are abstracted as parameters, i.e., we reflect the parameter values of other perspectives through explicit assumptions and simplifications in such models. Consequently, the resulting top model within each perspective can be coupled with its experimental frame to run simulations and derive results. Components of the various perspectives are integrated to provide a holistic view of the healthcare problem and system under study. The resulting global model can be coupled with a holistic experimental frame to derive results that cannot be accurately addressed in any of the perspective taken alone. Furthermore, as we endeavored to allow perspective-specific experts contribute to the modeling process, we took

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

	benefit of results originating from research efforts that Norbert Giambiasi initiated in the 2000's, which his PhD students further developed with their own PhD students.

SCHOLARONE™
Manuscripts

For Peer Review

Modeling and Simulation Framework for Value-based Healthcare Systems

Mamadou Kaba Traoré (1), Gregory Zacharewicz (2), Raphaël Duboz (3), Bernard Zeigler (4)

(1) LIMOS CNRS UMR 6158, Université Clermont Auvergne, France

(2) IMS-LAPS UMR CNRS 5218, Université de Bordeaux, France

(3) IPC, Cambodia and CIRAD UMR ASTRE, Montpellier, France

(4) ACIMS, University of Arizona, USA

Abstract

Regardless of the coordination of its activities, a healthcare system is composed of a large number of distributed components that are interrelated by complex processes. Understanding the behavior of the overall system is becoming a major concern among healthcare managers and decision makers. This paper presents a modeling and simulation framework to support a holistic analysis of healthcare systems through a stratification of the levels of abstraction into multiple perspectives and their integration in a common simulation framework. In each of the perspectives, models of different components of healthcare system can be developed and coupled together. Concerns from other perspectives are abstracted as parameters, i.e., we reflect the parameter values of other perspectives through explicit assumptions and simplifications in such models. Consequently, the resulting top model within each perspective can be coupled with its experimental frame to run simulations and derive results. Components of the various perspectives are integrated to provide a holistic view of the healthcare problem and system under study. The resulting global model can be coupled with a holistic experimental frame to derive results that cannot be accurately addressed in any of the perspective taken alone. Furthermore, as we endeavored to allow perspective-specific experts contribute to the modeling process, we took benefit of results originating from research efforts that Norbert Giambiasi initiated in the 2000's, which his PhD students further developed with their own PhD students.

Keywords: value-based healthcare system, healthcare modeling and simulation, holistic analysis, model integration, experimental frame

1. Introduction

The objectives of value-based healthcare can be broadly stated by the following equation:

$$\text{Objectives} = \text{low Cost} + \text{high Quality} + \text{wide Accessibility} \quad (1)$$

The exact meaning of the attributes, Cost, Quality, and Accessibility can vary, as can their priority, or even applicability, in different contexts. Nevertheless, when we refer to measuring value we mean some concrete formulation of increase in quality, while reducing cost, and increasing access. The importance of equation (1) becomes evident when we recognize that a healthcare service system is composed of a large number of distributed components that are interrelated by complex processes. Understanding the behavior of the overall system is becoming a major concern among healthcare managers and decision-makers intent on increasing value for their systems.

Most of the work concerning healthcare system modeling and simulation (M&S) in the literature is unit or facility specific. This is revealed in numerous research efforts published

over many decades seeking to provide support for healthcare system management in efficient use of resources for healthcare delivery. Indeed, literature review shows a huge number of research papers in the area of M&S applied to Healthcare management. Many of these efforts concentrate on one of the 4 generic perspectives we've identified in the framework proposed. Some of them integrate 2 or 3 of these perspectives. To our knowledge, none of them integrates all 4 perspectives in one global view. Therefore, such efforts cannot provide the necessary big picture for a fine-grained understanding of issues.

This paper takes a holistic approach to healthcare. It presents a framework that encompasses common perspectives taken in the research literature but also goes beyond them toward their integration with additional perspectives that are becoming critical in today's environment. It proposes a stratification of the levels of abstraction into multiple perspectives. In each of these perspectives, models of different components of healthcare systems can be developed and coupled together. Concerns from other perspectives are abstracted as parameters in such models. An important element of this approach is that we attempt to reflect the parameter values of other perspectives through explicit assumptions and simplifications. Consequently, the resulting top model within each perspective can be coupled with its experimental frame to run simulations and derive predictions of value outcomes for various alternatives tried. Components of the various perspectives are integrated to provide a holistic view of the healthcare problem and system under study. The resulting global model can be coupled with a holistic experimental frame to derive results that cannot be accurately addressed in any of the perspectives if taken alone. Moreover, the entire modeling effort is made easier by the integration, on top of our framework, of a workflow-based M&S approach that emanates from research works, which were initiated by Norbert Giambiasi and were furtherly developed by members of his team (Giambiasi et al., 2000), (Zacharewicz et al., 2008), (Bazoun et al., 2014). This approach consists in the disciplined design of a workflow model and its systematic transformation into a DEVS-based simulation model according to well-defined rules. Such an approach, when integrated to our framework, allows perspective-specific experts bring their knowledge at the conceptual level, while the transformation of the corresponding workflow model turns them into components of the framework.

The remaining of this paper is organized as follows. Section 2 presents the ontology that lays down the basis for our framework. Section 3 introduces the framework proposed. By connecting to research results previously established by Giambiasi's team members, section 4 illustrates how this framework can support an effective model-driven M&S engineering methodology. Section 5 discusses related research works and section 6 concludes the paper.

2. Ontology for healthcare systems simulation

Modeling healthcare systems is a quite challenging task, and especially knowing where to start and where to end. There is a wide variety of healthcare systems around the world, and every country's healthcare system reflects its own history, politics, economy and national values, that all vary to some degree. Nevertheless, some common levels of details can be considered when modeling the entire domain of healthcare. This is where ontology comes into play.

In the field of healthcare, Okhmatovskaia et al. (2012) introduced ontology for simulation modeling of population health (SimPHO), an explicit machine-readable specification of a domain of knowledge integrating both aspects of taxonomy and vocabulary in a form of

logical axioms. Silver et al. (2007) developed an ontology-driven simulation model that promotes relationship between domain ontology and simulation ontology. The resulting models are then translated into executable simulation models that can be used by simulation tools. Zeshan & Mohamad (2012) presented domain ontology for Information Technology (IT)-based healthcare systems that support knowledge sharing between devices and actors during the diagnostic process of patients in emergency departments. Puri et al. (2011) proposed ontology mapping and alignment to integrate ontologies from heterogeneous sources together and to support data integration and analysis. Literature review teaches two major lessons: (1) healthcare modeling and simulation covers more than one system perspective; (2) the entire domain suffers from the lack of standards and formal specification of agreed-upon concepts and their relationships to derive holistic simulation models.

We propose the Ontology for Healthcare Systems Simulation (O4HCS), a formal specification of relevant concepts and their relationships in healthcare domain designed to build holistic healthcare simulation models (Figure 1). When developing O4HCS, it is essential that we provide, at some general level, a formal framework that captures all the knowledge that might be in the range of healthcare M&S that the ontology is likely to be used for (Partridge et al., 2013). For this reason, we use the System Entity Structure (SES) framework (Zeigler, 1984).

2.1. SES Ontological Framework

SES enables fundamental representation of hierarchical modular model providing a design space via the elements of a system and their relationships in hierarchical and axiomatic manner. It is a declarative knowledge representation scheme that characterizes the structure of a family of models in terms of decompositions, component taxonomies, and coupling specifications and constraints. SES supports development, pruning, and generation of a family of hierarchical simulation models. It is a formal ontology framework, axiomatically defined, to represent the elements of a system (or world) and their relationships in hierarchical manner.

Figure 1 provides a quick overview of the nodes and relationship involved in a SES. Entities represent things that have existence in a certain domain. They can have variables which can be assigned a value within given range. An Aspect expresses a way of decomposing an object into more detailed parts and is a labeled decomposition relation between the parent and the children. Multi-Aspects are aspects for which the components are all of the one kind. A Specialization represents a category or family of specific forms that a thing can assume. It is a labeled relation that expresses alternative choices that a system entity can take on.

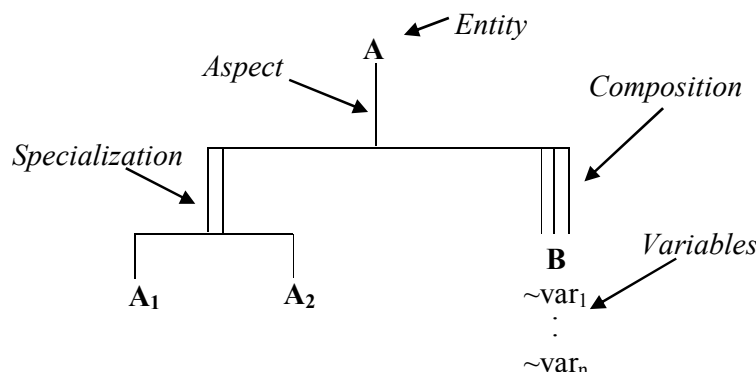


Figure 1. Basic SES Construction

SES has six axioms (Zeigler & Sarjoughian, 2017): uniformity, strict hierarchy, alternating mode, valid brothers, attached variables and inheritance. Uniformity forces that any two nodes with the same labels have isomorphic subtrees. Strict hierarchy prohibits a label from appearing more than once down any path of the tree. Alternating mode states that, if a node is an Entity, then the successor is either Aspect or Specialization, and vice versa. Valid brothers forbids having two brothers with the same label. Attached variables constraints that variable types attached to the same item shall have distinct names. Inheritance asserts that Specialization inherits all variables and Aspects from the parent Entity to the children Entities. Zeigler & Hammond (2007) provide a formal set-theoretic characterization of the SES that shows how the axioms are satisfied.

SES is targeted to support the plan-generate-evaluate process in simulation-based systems design. The plan phase recaptures all the intended objectives of the modeler while the generate phase reproduces a candidate design model that will meet the initial objectives. The evaluate phase assesses the performance of the generated model through simulation. As such, SES organizes a family of alternative models from which a candidate model can be generated, selected and evaluated through system design repeatedly until the model meets an acceptable objective. While complex systems are composed of large components and their structural knowledge can be broken down and systematically represented in SES, their behaviors can be specified in either atomic or coupled models and saved in model base (an organized library) for later use. Once the models are saved they can be retrieved from their repository and reused to design complex systems.

2.2. O4HCS Model

We adopted a useful way to begin building O4HCS by surveying existing taxonomies of healthcare models as offered by (Brailsford, 2007), (Gunal & Pidd, 2010), and (Roberts, 2011). Consequently, O4HCS is built based on an extensive literature review of healthcare simulation and the use of expert knowledge. Contrary to the existing ontologies, the purpose of O4HCS is not to address the lack of unified vocabulary in health or clinical medicine. Instead, the development of O4HCS is an attempt to share among simulation experts and domain experts, a common understanding of the abstractions necessary/used for the simulation of the entire healthcare domain (beyond unit specific and facility specific modeling), as well as to serve as a support for the plan-generate-evaluate process mentioned earlier.

The following are expressed by Figure 2:

- Healthcare is often treated in literature at different levels of care including primary care level, secondary care level, tertiary care level, and home (& community) care level.
 - Primary care is a first point of consultation for patients, where professionals are general practitioners, family physicians, nurses and assistants, who operate in multiple settings like primary care centers, provider offices, clinics, schools, colleges, prisons, and worksites.
 - Secondary care more often is referred to as hospital units, like emergency department or medical imaging block, where specialists like cardiologists,

- urologists and dermatologists provide acute care, i.e., necessary treatments for a brief but serious illness, injury or other health condition.
- Tertiary care addresses specialized consultative health care in advanced medical investigation and treatment, like cancer management, advanced neonatology services, and complex medical and surgical interventions.
 - Home care (often associated to community care) is concerned with public health interest, such as food safety surveillance, distribution of condoms, or needle-exchange campaign, usually outside of health facilities. It also includes support to self-care, assisted living, and other types of social care services.
- A healthcare system is made of one or various organizations, each of which being a production system, a consumption system, or a coordinating system between production and consumption. As noticed in (Brailsford et al., 2011), literature contains a vast number of models for the demand and the supply of health care services, although these models have mainly focused on specific conditions (and in some cases on specific locations). More recent works have focused on the coordination dimension (Redding et al., 2014), (Zeigler et al., 2014).
 - Healthcare production has two facets:
 - The first one deals with how resources are transformed into services. Resources include physical resources (e.g., buildings, rooms, beds, drugs, vaccines or equipment), human resources (e.g., physicians, nurses, or assisting personnel), financial resources (e.g., donations, taxes, or out-of-pocket payments), and information (e.g., medical records, training documents, or advertisement materials). Models of such transformation explicitly describe the dynamics of the provider (e.g., the economic model of health funding, which can be tax/out-of-pocket/insurance-based, or the information system as the health data provider), or the provision (e.g., the clinician as a human resource), or both. Examples are (Ozcan et al., 2011), (Verma & Gupta, 2013), (Khurma et al., 2013), (Sobolev et al., 2008), (Kuhl, 2012), (Bountourelis et al., 2011), (Marmor et al., 2011), (Cote, 1999), (Viana et al., 2012), (Findlay & Grant, 2011).
 - The second facet deals with the generation of health phenomena, whether positive or negative. Positive phenomena (like vaccination campaign) produce ease, while negative phenomena (like disease spreading) produce disease. Diffusion processes are classically described as either spatial or functional phenomena. The former explicitly describe space (e.g., cellular automata-based models), and the resources involved (e.g., attributes of the cellular automata's cells can be models in their turn), while the latter formulate the dynamics of the diffusion process in the form of mathematical equations (e.g., compartmental models such as SIR, SEIRD...). Producer systems models focus on health producers and their provision of health services, and abstracts processes from any other aspect by parameters. Illustrative examples are disease outbreak models (Kasaie et al., 2013), (Dibble, 2010).
 - The demand for health is generated by a population or individuals who seek for care in times of need. Hence, M&S models of consumption systems focus on those health consumers and the dynamics of their demands, and abstract by parameters all processes from any other aspect.
 - A Population dynamics model is related to births, deaths and demographic flows such as immigration and emigration. It is either expressed as equations, i.e., functional dynamics (Bohk et al., 2009), or considered as an emerging

- phenomenon composed of individuals geographically located in a space model, i.e., spatial dynamics.
- An individual can be modeled as an autonomous entity with specific attributes, and a behavior driven by goals, including social dimensions. Typical examples are agent-based models (Charfeddine & Montreuil, 2010), (Onggo, 2012), (Ramirez-Nafarrate & Gutierrez-Garcia, 2013), and (Davis et al., 2013). An alternative modeling approach is to describe the flow of activities that captures scenarios the individual can undergo (such as patient flow models).
 - Care coordination can be seen as cross-organization coordination managing the entities and resources of existing ones. It is needed to the extent that existing organization is lacking. Pathways are means to do that coordination (Zeigler, 2017).

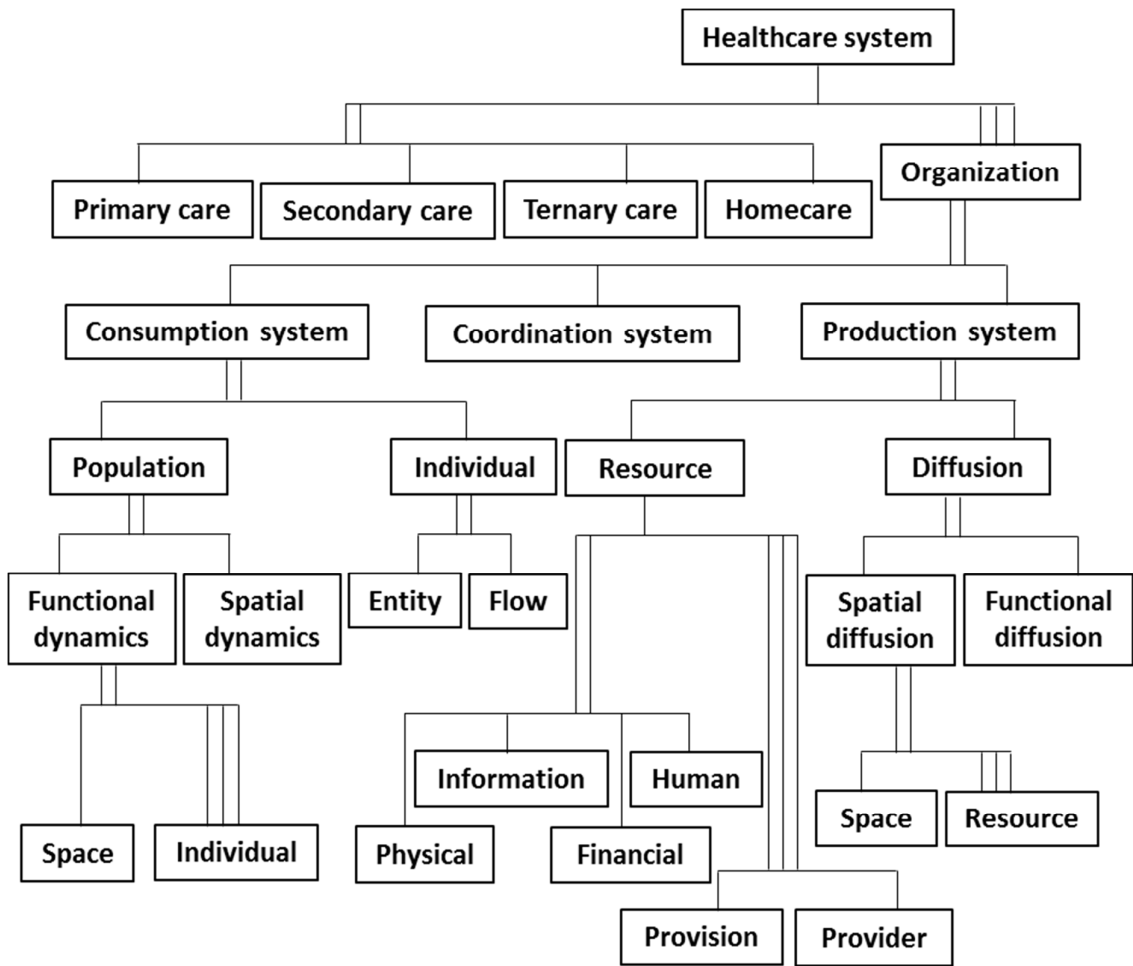


Figure 2. Ontology for Healthcare Systems Simulation (O4HCS)

3. Ontology-driven M&S framework

More often, modelers are confronted with the challenge of developing simulation models for efficient design and analysis of healthcare systems. As it turns out, the underlying components are studied in isolation focusing on either unit specific or facility specific. O4HCS ontology reflects a disciplined stratification of concerns and a systematic description of the interactions

that exist between them, from which we derive a 4-layered framework for multi-perspective modeling and holistic simulation of healthcare systems (as depicted by Figure 3).

This way, we distinguish 4 fundamental perspectives that simulation models develop, either, one at a time, or by combining two or more of them. The layers of our framework cover the full set of healthcare concerns, which, though interrelated, are often treated separately and the impact of other concerns on any one of them being approximated by parameters. We place this stratification of abstractions in the context of the hierarchy of systems specification introduced by (Zeigler, 1976). That way, each perspective can be seen as encompassing a family of questions that can be formulated through dedicated experimental frames (Zeigler, 1984). Consequently, models can be developed within each perspective and coupled together. The resulting top model in each perspective can be coupled with its experimental frame to derive results specific to this perspective:

- The **Resource Allocation** (RA) perspective encompasses all scheduling and planning problems, mostly in the context of limited resource provisions, to meet the healthcare demand. RA models are used to answer questions formulated through RA-specific experimental frames. Examples of such questions are the occupancy rate of beds in a surgical unit, the average waiting time in an emergency department, or the optimal scheduling of health care activities (Harper, 2002), (Augusto & Xie, 2014), (Viana et al., 2012), (Zulkepli et al., 2012), (Fletcher et al., 2009), (Bountourelis et al., 2011), (Cote, 1999), (Ahmed & Alkhamis, 2009).
- The **Health Diffusion** (HD) perspective covers simulation studies of ease/disease spreading. HD-specific experimental frames are coupled to HD models, in order to derive answers for questions such as the forecasted proportion of individuals in a population according to their health status, or the patterns of contamination areas from given initial conditions (Bisset et al., 2012), (Macal et al., 2012), (Okhmatovskaia et al., 2012), (Ferranti & Freitas Filho, 2011).
- The **Population Dynamics** (PD) perspective comprises all studies of the dynamics in the population of a community (immigration, emigration, birth, death...). PD-specific experimental frames formulate summary mappings to answer questions like the forecasted distribution of a population by gender, social status or age range, or the impact of a species strategy on the encapsulating ecosystem (Allen, 1976), (Bohk et al., 2009), (Leslie, 1945), (Sheppard, 1985), (Sikdar & Karmeshu, 1982).
- The **Individual Behavior** (IB) perspective covers the studies of social behavior in relation to how its components (such as educational level, physical state, emotion, cognition, decision...) affect the willingness/ability of an individual to effectively access available healthcare services. IB-specific experimental frames address questions such as the relationship between socio-cultural decisions and health status of individuals, or the evaluation of life strategies in the context of competition/selection and scarcity of resources (Charfeddine & Montreuil, 2010), (Ramirez-Nafarrate & Gutierrez-Garcia, 2013), (Kasaie et al., 2013).

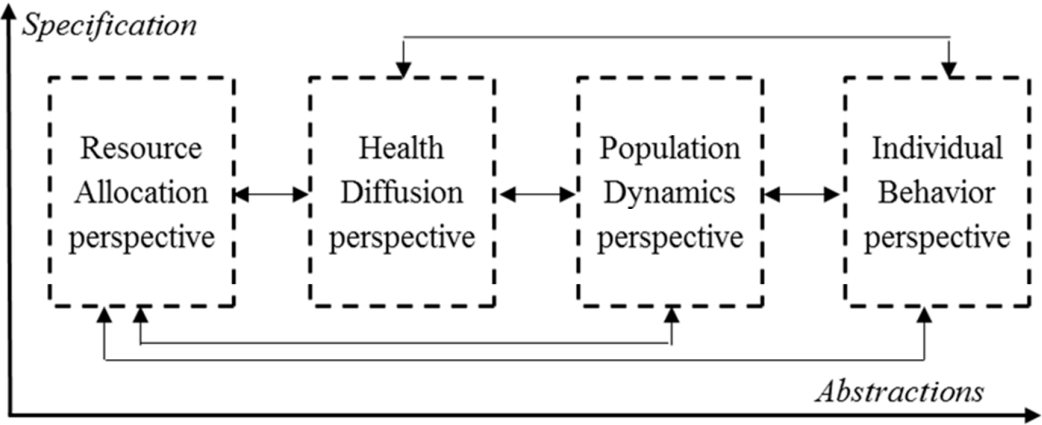


Figure 3. Multi-perspective approach to healthcare systems M&S

While this feature provides multiple levels of explanation for the same system, there is also the need to encompass the influences of perspectives on one another. While the dashed boxes in Figure 3 depict independent simulations in the different perspectives, the double arrows represent the live exchanges of information between them. *The idea is to allow for the transmissions of the outputs of the simulations in one perspective to provide live feedbacks to the simulation parameters in other perspectives where required.* We have defined an integration mechanism to enable such exchange as detailed in the next sub-section.

3.1. Holistic approach

In practice, M&S processes in each of the identified perspectives are executed in isolation; i.e. without recourse to the processes from other perspectives. In reality, however, processes usually have mutual influences. For instance, when there is an epidemic in a community (HD perspective), it will naturally affect the provisions and allocations of the human and infrastructural healthcare resources in the health centers within the community (RA perspective) and the migrations of people into and out of the community (PD perspective). To allow a holistic simulation, which encompasses isolated perspective-specific simulations and their mutual influences, we suggest an integration mechanism to enable live exchanges of information between models from the different perspectives.

However, while models within the same perspective are coupled the classic way (i.e., outputs to inputs) to form larger models within the same perspective, models from distinct perspectives relate in a different way. Indeed, the parameters of a focused model in a given perspective are fed by the outputs of models from other perspectives. In other words, these outputs provide a disaggregated understanding of the phenomena approximated by the parameters of the focused model. Technically, this is realized by creating a model which activity is to translate outputs received from the other models into new values for the parameters of the focused model.

Our approach is very comparable to the one introduced in (Seck & Honig, 2012), where the model used to realize the integration is called a bridging model. However, there is a major difference in that we don't allow the output of a model in a given perspective to feed the input of another model in a different perspective. The reason is that inputs and outputs of models are defined based on the perspective envisioned, which also set the family of objectives of the

corresponding M&S study. Any process, which output can feed such inputs or which input can be fed by such outputs, is an abstraction within that perspective. Abstractions from other perspectives are solely captured by model parameters.

Figure 4 schematizes the technical difference between “coupling” and “integration” in the context of this work. By coupling the output of a disease-spreading model to the input of an integrator, we create a coupled model in the HD perspective. The role of this integrator is to interpret the outputs received from the disease model and translate it into new values for the parameters of a population dynamics model. The integrator will then call the method of the PD model to modify its parameters. Similarly, the population dynamics model is coupled to an integrator that translates its output to values for the parameters of the disease-spreading model. A holistic model of the healthcare system is obtained by introducing appropriate integrators between perspective-specific models.

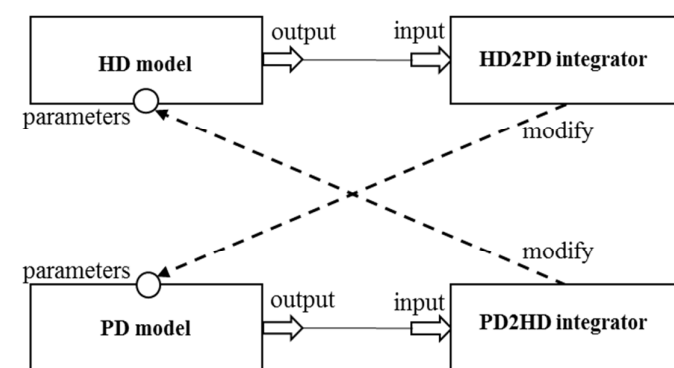


Figure 4. Holistic approach to healthcare systems M&S

3.2. Formalization of the framework

Contrary to (Seck & Honig, 2012), we see a significant difference between the receipt of input by a model and the modification of its parameter. Viewing a simulation model as a transition system (as done in DEVS), the semantics of the first one is that stimuli coming from the model’s environment provoke a change of the model’s internal state, and this change is governed by the model’s transition rules (external transition, in the case of DEVS). The semantics of parameter modification is that knowledge revealed from another reality of the system modeled provokes a change of the model’s internal rules (instead of its state). Let us clarify this, in the framework of DEVS M&S.

The DEVS M&S framework (Zeigler, 1976) suggests a specification hierarchy to capture the knowledge specific to systems structure and behavior. Each level has an associated set-theoretic structure (n-tuple) that allow to describe a system. Going up the hierarchy (from behavior to structure) adds more elements to the n-tuple, since we know more about the system as levels increase. There are corresponding morphisms at each level, i.e., how to tell whether two descriptions of the same system at a level are equivalent or related at that level. Also, the morphisms at one level are consistent with those below, i.e., if two descriptions are equivalent at a higher level, then they are also equivalent at every lower level. Going down the levels is computationally done by simulation, while going up the levels (also known as structural inference) is much harder and can be realized under justifying conditions. On top of the hierarchy is the Coupled Network (CN) level, below which is the Input Output System (IOS) level. Models expressed at the CN level are called coupled models, while the ones

expressed at the IOS level are called atomic models. Simulation modelers usually describe their models at those levels using code equivalents (depending on the programming language) of the set-theoretic specifications given below. These levels are often the most convenient to describe the *structure* of the system under study, while the well-defined DEVS simulation algorithms generate the *behavior* of these models which is described lower levels of the hierarchy.

An atomic model is defined by the n-uple $\langle X, Y, S, \delta_{\text{int}}, \delta_{\text{ext}}, \delta_{\text{conf}}, \lambda, \text{ta} \rangle$ where :

- X, Y and S are respectively the input set, output set, and state set (at any time, the system modeled is in one of the possible states)
- $\text{ta} : S \rightarrow \mathcal{R}_0^{+\infty}$ is the time advance function (i.e., it gives the lifespan of each state), with $\mathcal{R}_0^{+\infty}$ designating the set of non-negative real numbers, including $+\infty$
- $\delta_{\text{int}} : S \rightarrow S$ is the internal transition function (i.e., it is triggered only when the elapsed time in the system's current state s_{curr} has reached $\text{ta}(s_{\text{curr}})$ without the system being disturbed by any receipt of input)
- $\lambda : S \rightarrow Y$ is the output function (i.e., it computes the output of the system, each time an internal transition is occurring)
- $\delta_{\text{ext}} : Q \times X \rightarrow S$ is the external transition function (i.e., it is triggered only when the system receives an input, while the elapsed time in the system's current state s_{curr} has not reached $\text{ta}(s_{\text{curr}})$), and $Q = \{(s, e) / s \in S, 0 \leq e < \text{ta}(s)\}$ is called the total state
- $\delta_{\text{conf}} : S \times X \rightarrow S$ is the confluent transition function (i.e., it is triggered only when the system receives an input at exactly the time that the elapsed time in the system's current state s_{curr} has reached $\text{ta}(s_{\text{curr}})$)

If an atomic model is parameterized, its parameters are disjoint from its state variables. Parameters are constant values the model will refer to when triggering its transition functions or when computing its outputs, or even when determining its time advance. Therefore, any change of value of a parameter results in a change of the model's internal rules (and not a state transition). This is akin to dynamic structure change – See (Muzy & Zeigler, 2014) for a recent review of dynamic structure DEVS. It takes us away from the multi-perspective formalization proposed in (Seck & Honig, 2012) and calls for another formalization approach.

We define a *parameterized atomic DEVS* as an atomic DEVS model deriving from an existing atomic DEVS model. It is defined by $\langle X^P, Y^P, S^P, \delta_{\text{int}}^P, \delta_{\text{ext}}^P, \delta_{\text{conf}}^P, \lambda^P, \text{ta}^P \rangle$, where:

- P is the parameters set (each element of P is a vector of values of parameters)
- $\langle X, Y, S, \delta_{\text{int}}, \delta_{\text{ext}}, \delta_{\text{conf}}, \lambda, \text{ta} \rangle$ is an atomic model whose governing functions depend on P (i.e., they compute their values, using the values of P), called the *strain* model.
- $X^P = X \times P$
- $Y^P = Y$
- $S^P = S \times P \times \mathcal{R}_0^{+\infty}$
- $\text{ta}^P : S^P \rightarrow \mathcal{R}_0^{+\infty}$
 $\text{ta}^P(s, p, \sigma) = \sigma$
- $\delta_{\text{int}}^P : S^P \rightarrow S^P$
 $\delta_{\text{int}}^P(s, p, \sigma) = (\delta_{\text{int}}(s), p, \text{ta}(s))$
- $\lambda^P : S^P \rightarrow Y^P$
 $\lambda^P(s, p, \sigma) = \lambda(p(s))$
- $\delta_{\text{ext}}^P : Q^P \times X^P \rightarrow S^P$, with $Q^P = \{(s, p, \sigma, e) / (s, p, \sigma) \in S^P, 0 \leq e < \sigma\}$
 $\delta_{\text{ext}}^P(s, p, \sigma, e, \emptyset, q) = (s, q, \sigma - e)$

$$\begin{aligned}
& \delta_{\text{ext}}^P(s, p, \sigma, e, x, \emptyset) = (\delta_{\text{ext}P}(s, e, x), p, \text{ta}_P(\delta_{\text{ext}P}(s, e, x))) \\
& \delta_{\text{ext}}^P(s, p, \sigma, e, x, q) = (\delta_{\text{ext}P}(s, e, x), q, \text{ta}_q(\delta_{\text{ext}P}(s, e, x))) \\
& \bullet \delta_{\text{conf}}^P : S^P \times X^P \rightarrow S^P \\
& \delta_{\text{conf}}^P(s, p, \sigma, x, \emptyset) = (\delta_{\text{conf}P}(s, x), p, \text{ta}_P(\delta_{\text{conf}P}(s, x))) \\
& \delta_{\text{conf}}^P(s, p, \sigma, x, q) = (\delta_{\text{conf}P}(s, x), q, \text{ta}_q(\delta_{\text{conf}P}(s, x)))
\end{aligned}$$

The parameterized model is an embedding structure for a strain atomic model. It distinguishes inputs that impact on the strain model's state from inputs that only modify the values of parameters. A variable is defined (σ) to memorize the remaining time in any current state of the strain model (i.e., time before the lifespan expires). Hence, this variable gives the time advance function of the parameterized model. The internal transition of the parameterized model changes the state of the strain model according to its internal transition function, but does not affect the parameters. The output sent at that time is the one computed by the strain model. When only new values for parameters are received by the parameterized model, the state of the strain model is kept unchanged, and only the remaining time is updated. When only input values impacting the strain model's state are received (without input for modification of parameters), the new situation is defined by the strain model's external transition and time advance function. When both input values impacting the strain model's state, and input for modification of parameters are received, the new situation is defined by the strain model's external transition and time advance function; the new state of the strain model is computed based on the current values of parameters, but the lifespan of this new state is computed using the new values of parameters. The same rules apply for confluent transition.

With such a formalization, a multi-perspective model (i.e., resulting from the holistic approach presented) can be given at the CN level of the systems specification hierarchy. A coupled model is defined by $\langle X_{\text{self}}, Y_{\text{self}}, D, \{M_d\}_{d \in D}, \{I_d\}_{d \in D}, \{Z_{i,j}^P\}_{i \in D \cup \{\text{self}\}, j \in I_i} \rangle$ where:

- X_{self} and Y_{self} are respectively the input set and the output set
- D is the set of references of the model's components
- M_d is a model component, an atomic or a coupled model, with X_d and Y_d as respectively its input and output set
- I_d is the influence set of component d , i.e., all other models sending input to d
- $Z_{\text{self},d} : X_{\text{self}} \rightarrow X_d$ is the external input transfer function (which indicates how input received by the coupled model are transferred to its component models)
- $Z_{d,\text{self}} : Y_d \rightarrow Y_{\text{self}}$ is the external output transfer function (which indicates how output generated by the component models are transferred to the coupled model)
- $Z_{i \in D, j \in D - \{i\}} : Y_i \rightarrow X_j$ is the internal transfer function (which indicates how output generated by the component models are transferred to other component models)

We similarly define a parameterized coupled model as a coupled DEVS model deriving from a strain coupled model, by $\langle X_{\text{self}}^P, Y_{\text{self}}^P, D^P, \{M_d^{Pd}\}_{d \in D}, \{I_d^{Pd}\}_{d \in D}, \{Z_{i,j}^P\}_{i \in D \cup \{\text{self}\}, j \in I_i} \rangle$ where:

- $X_{\text{self}}^P = X_{\text{self}} \times (\times P_d)_{d \in D}$
- $Y_{\text{self}}^P = Y_{\text{self}}$
- $D^P = D$
- M_d^{Pd} is a parameterized DEVS model if $P_d \neq \emptyset$ (with $X_d^{Pd} = X_d \times P_d$ as its input set), and a "regular" DEVS model if $P_d = \emptyset$ (with $X_d^{Pd} = X_d$ as its input set)
- I_d^P includes all components models sending input to d , whether for parameter modification or internal state change
- $Z_{\text{self},d}^P : X_{\text{self}}^P \rightarrow X_d \times P_d$

- $Z_{self,d}^P(x, p) = ((Z_{self,d}(x), p_d)$
- $Z_{d,self}^P = Z_{d,self}$
- $Z_{i \in D, j \in D - \{i\}}^P : Y_i \rightarrow X_j \times P_j$
- $Z_{i \in D, j \in D - \{i\}}^P(y) = (x, \emptyset)$ for a “regular” coupling
- $Z_{i \in D, j \in D - \{i\}}^P(y) = (\emptyset, p_j)$ for an “integration” (or a bridging)

3.3. Illustrative Application

In order to illustrate the proposed framework, we now present a study of the Nigerian healthcare system done in a holistic way. We applied our framework in the context of the Ebola outbreak and built models in each of its perspectives, i.e.:

- a model of the Ebola outbreak and its experimental frame (HD perspective),
- a model of migrations between Nigerian states and its experimental frame (PD perspective),
- a model of daily workers strategy and its experimental frame (IB perspective), and
- a model of hospital resource allocation in Lagos and its experimental frame (RA perspective).

We studied each model in isolation and derived perspective-specific results, and then integrated all the models together to produce a holistic view of the situation. Interested readers will find a description of these models in the appendix (in their initial forms, which have later been transformed into their DEVS counterparts).

Figure 5 top shows the four perspective-specific models with rough indications of their parameters (red arrows) and state variables (blue arrows.) Each of these models can be given default parameters which remain constant and generate dynamics of their state variables. These can be taken as characterizing normal endogenous activity unperturbed by an exogenous event such as an Ebola outbreak. Figure 5 bottom gives more detail in the form of a causal loop diagram of the influence of state variables on parameters. For example, the transmission rate of Ebola virus is negatively impacted by more hospital admissions and positively increased as the population of a state or locality is increased.

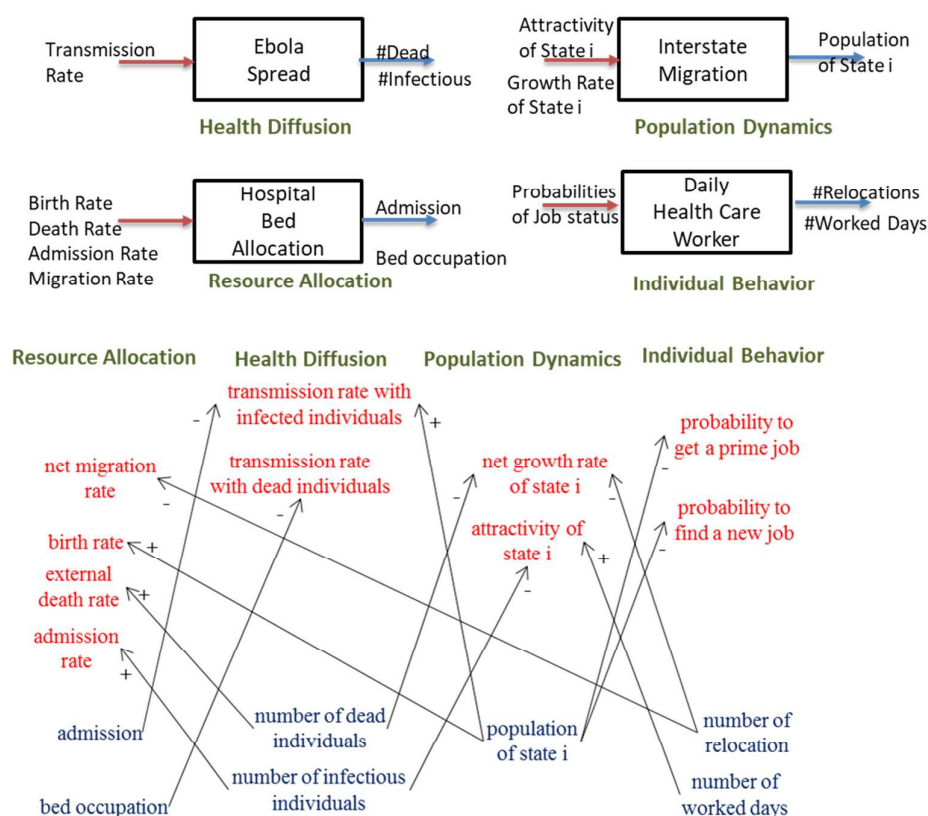


Figure 5. Holistic Multi-perspective Model of Ebola Outbreak

The experimental frame built to experiment with the resulting holistic model allows us to see how all models impact on each other simultaneously, and in various scenarios of influence.

Figure 6 shows results for the case where the influence relations of Figure 5 are treated as linear functions mapping from state variable values to parameter values:

- Top left curves show the distribution of population over a period of 100 days, depending on the health status of individuals (dark blue curve for susceptible individuals, red curve for exposed individuals, green curve for infected individuals, purple curve for recovered individuals, and light blue curve for dead individuals).
- Top right curves show, during the same period of time, the impact of daily workers decision on their job performances (the blue curve indicates the frequency of relocations of the worker, from a working area to another one, while the red curve indicates the ratio of worked days over the total number of days spent).
- Bottom left curve shows the daily evolution of the population in Lagos state at the time of the outbreak, while bottom right curve shows the ratio of bed occupancy in proportion of the population in the focused Lagos hospital, at the same time.

Interestingly, although not illustrated here, the movement of health care workers between locations which is guided by their perception of available jobs may not result in optimal assignments. Such results of holistic modeling point to aspects where coordination as supported by pathways (Zeigler et al., 2014) may result in improved performance.

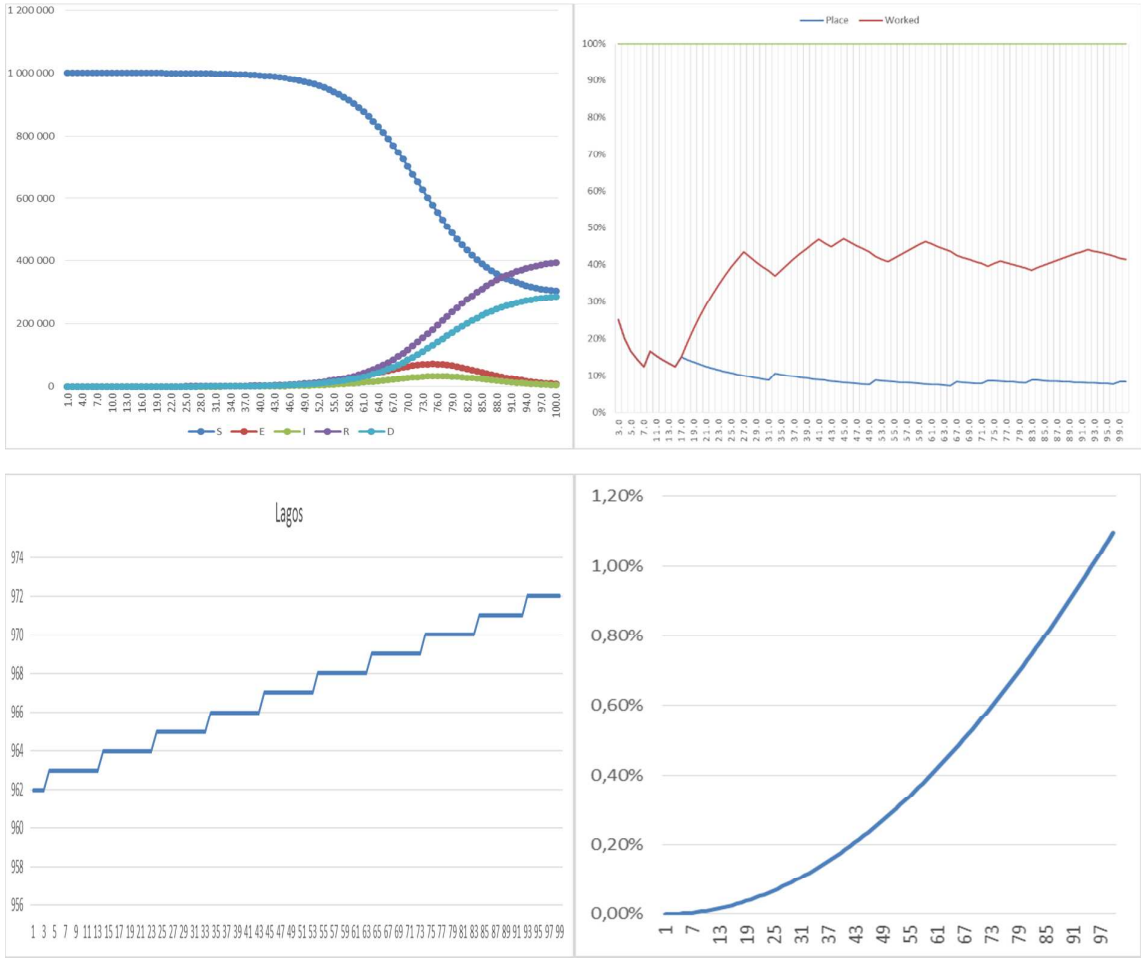


Figure 6. Holistic simulation results

4. Collaborative Modeling to Multi-perspective Holistic Simulation

In the context of multi-perspective modeling to holistic simulation, a key issue is how to effectively capture the concerns of the various stakeholders involved and among whom the entire knowledge is broken down into partial information. For example, the Collaborative, Participative, Interactive Modeling (aka CPI Modeling) approach proposed in (Barjis, 2011) advocates for models being designed collaboratively with participation of the users and business process owners. This section connects our framework to a feature that support such an approach.

As shown by Figure 7, at the top-most level, a process-oriented model (called the workflow model) is used by collaborating domain experts to specify the bridge between various models built from the different perspectives. At lower levels, transformation rules are defined to generate the DEVS-based multi-perspective model. Each perspective-specific model is turned into its DEVS counterpart, or directly selected in a DEVS-oriented model base. The integration relations are translated into DEVS bridging models as indicated previously.

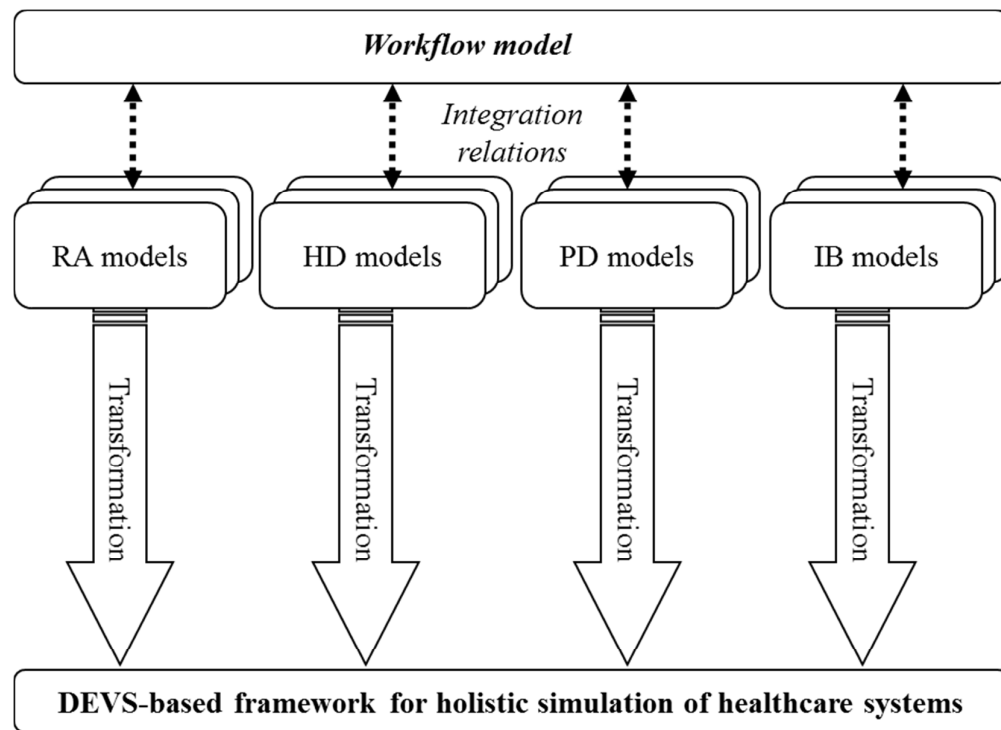


Figure 7. Collaborative modeling approach to holistic simulation

The design of the workflow model, as well as its transformation into DEVS models to serve as components of the framework, are based on research works initiated by Norbert Giambiasi with one of his PhD student and further developed by the latter and PhD students of his own. As detailed subsequently, this research effort started with classical workflow-based M&S, and then got matured with BPMN-based M&S.

4.1. Workflow Modeling and Simulation

Workflows have been developed in several domains such as production science, information systems, scientific protocols, etc. As a major investigator since the middle of the 90's, the Workflow Management Coalition (WfMC) has developed an XML-based language to represent workflows (XML Process Definition Language, XPDL), which became a standard in the community (Hollingsworth, 1995), (WMC, 1999). Workflows have been coupled with simulation features (Van der Aalst & Van Hee, 2002). In works led by Norbert Giambiasi (Zacharewicz et al., 2008), XPDL models describe composite items (e.g. patient cases) passing over a sequence of treatments, task components that treat items, and controller components that route items between tasks. These models are transformed into coupled G-DEVS models (Giambiasi et al., 2000) in a three-step method (Zacharewicz et al., 2008). Each basic component of an XPDL model is translated into a GDEVS atomic model. G-DEVS was chosen for its capacity to handle in one event a list of values. This list was smartly carrying information about the product or flow and it was used to route the flow and track information. All the G-DEVS atomic models are then coupled together to form the DEVS-based simulation model of the entire XPDL model. This method has successfully been applied to the industrial manufacturing processes of electronic components.

4.2. BPMN Modeling and Simulation

After a decade of maturity, workflow modelers started looking for a more comprehensive and user friendly language. The combined efforts of working groups such as Business Process Initiative (BPI) and the Object Management Group (OMG), led to BPMN (Business Process Modeling Notation), a graphical, high level, and user friendly process description language (OMG, 2011). BPMN is associated to BPEL (Business Process Execution Language) for its execution. In the context of M&S, authors in (Cetinkaya et al., 2012) and (Mittal et al., 2007) presented a Model Driven Development framework (called MDD4MS) for BPMN to DEVS transformation. BPMN is used at the conceptual modeling level and DEVS is used at the simulation modeling level. BPMN and DEVS Meta-models are defined and the former mapped onto the latter through a set of transformation rules. Basic concepts in BPMN, such as Task, Event, and Gateway, are transformed into DEVS atomic models, while more advanced concepts, such as Pool, Lane, and Sub Process, are transformed into DEVS coupled models. An alumnus from Giambiasi’s research group, in association with his own students and colleagues extended this approach to BPMN 2.0 (Bazoun et al., 2014).

4.3. Illustrated example

This simple example is to show intuitively how the process-oriented M&S approach developed in (Zacharewicz et al., 2008) and matured in (Bazoun et al., 2014) can easily connect to the M&S framework for value-based healthcare systems proposed. The BPMN model presented in Figure 8 describes a simple medical practice workflow and focuses on 3 different generic entities: Patient, Emergency Practitioner, and Medical Specialist. The two latter belong to a same Hospital. Figure 8 encompasses, in the form of a workflow, two perspectives of the framework proposed: the Patient entity is viewed from the IB perspective, while the pair, made of the Emergency practitioner and the Medical Specialist, are seen from the RA perspective. According to transformation rules defined in (Bazoun et al., 2014), the IB entity will turn into a DEVS atomic model, while the RA pair of entities will turn into a DEVS coupled model. Bazoun et al. (2014) defines an approach to transforming BPMN models into DEVS simulation models based on the metamodel approach. XML and ATL transformation mechanisms (Jouault et al., 2008) are used to obtain DEVS models, then the obtained DEVS are enriched by performance indicators (time and costs). Each patient model in Figure 8 represents an individual in the population, who is affected by a health issue. The model stresses the BPMN tasks (colored in orange) and the intermediate event that trigger the search for medical resources according to health regulation recommendations or procedures, and based on the type of health issue experienced. In the scenario described here, the patient is selecting the hospital emergency department (H) rather than a general practitioner (GP). The criteria used to do this selection are based on population dynamics-related knowledge (including geographical location, social status, etc.) abstracted by parameters. The outcome of the selection will, in its turn, feed parameters of RA-specific models. This feeding and the feedback received are materialized by the events sent between the Patient and the Emergency practitioner model. The result is affecting the patient health status both in IM and PD perspectives. Interested readers to detailed transformation rules are invited to refer to (Bazoun et al., 2014).

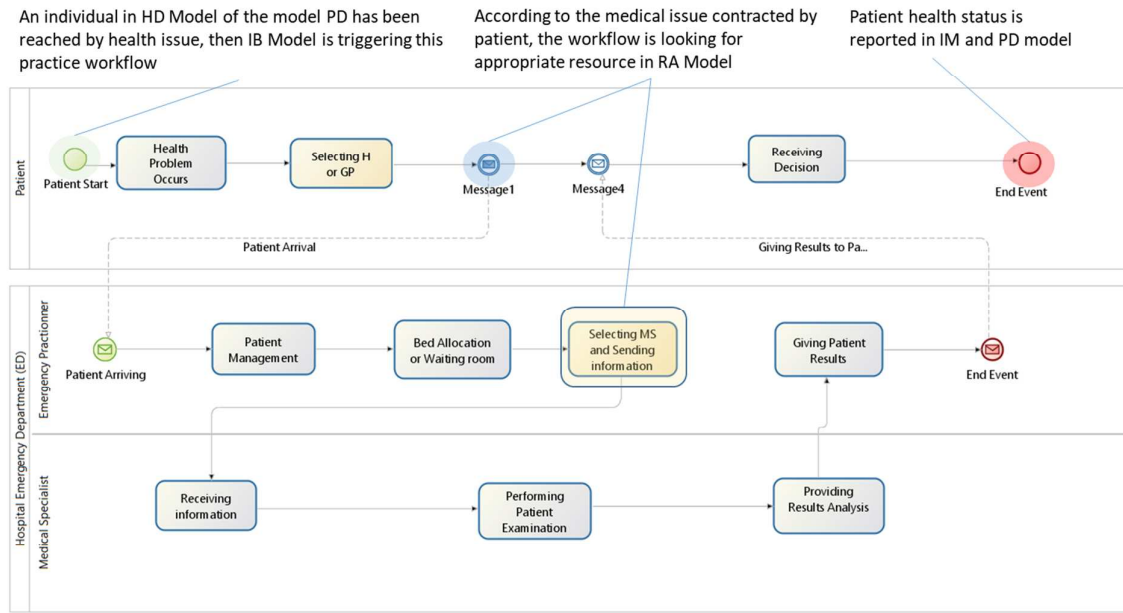


Figure 8. BPMN model of a medical practice workflow

5. Related works

Literature review shows a huge number of research papers in the area of M&S applied to Healthcare management. Many of these efforts concentrate on one of the 4 generic perspectives we have identified (Resource Allocation, Health Diffusion, Individual behavior, and Population Dynamics). Some of them integrate 2 or 3 of these perspectives. Table 1 shows a representative sample of such contributions. To our knowledge, none of them integrates the 4 perspectives in one holistic approach as does our framework.

Some previous works are close to our effort to propose a stratification of levels of abstraction and their integration into a holistic framework, though not identical. In (Charfeddine & Montreuil, 2010), the authors introduced a conceptual agent-based framework for modeling and simulation of distributed healthcare delivery systems, which is structured into a three-level categorization, with a simulation engine as the integration platform. The first layer includes Agents, Objects, Environment and Experience. In the second and the third layer, each component is broken down into two or more subcomponents with more details.

Table 1. Benchmark of integrated healthcare M&S frameworks

Integrated Healthcare M&S Frameworks	Resource Allocation	Health Diffusion	Population Dynamics	Individual Behavior
(Augusto & Xie, 2014)	✓			✓
(Viana et al., 2012)	✓	✓		✓
(Zulkepli et al., 2012)	✓			✓
(Bisset et al., 2012)		✓	✓	
(Macal et al., 2012)		✓		✓
(Harper, 2002)	✓			✓
(Okhmatovskaia et al., 2012)		✓	✓	
(Ferranti & Freitas Filho, 2011)		✓		✓

(Fletcher et al., 2009)	✓			✓
(Bountourelis et al., 2011)	✓			✓
(Bohk et al., 2009)			✓	
(Cote, 1999)	✓			✓
(Brailsford et al., 2003)			✓	✓
(Ahmed & Alkhamis, 2009)	✓			✓
(Weng et al., 2011)				
(Jeffers, 2014)	✓	✓	✓	

While seeking to provide methods to model an ideal healthcare delivery system viewed as loosely coupled distributed system of systems, (Zeigler et al., 2012) presented a methodology and modeling environment for simulating national health care based on multi-level modeling and families of models applicable to coordinated care architectures. The authors follow the approach of Aumann for the formulation of a hierarchical design in terms of a linearly ordered set of three levels, to define the primary (focal) level of model development and those levels immediately above and below together with their experimental frames. The authors developed a stratification of healthcare in four levels of Modeling Framework focused on coordination. Among the four levels, the level 2 which is the coordination of Individual’s Care in a Provider Group was the focal level for the immediately lower level that represents the patient adherence to provider’s care plan, and the next level up which is the coordinated care architectures of populations of patients and groups of providers. The upper fourth level represents the Healthcare Environment.

A taxonomy of healthcare models based on two simulation approaches, discrete-event simulation and system dynamics, was presented by (Brailsford, 2007) classifying models into three levels. At level 1 are models of the human body also called disease models, at level 2 are operational and tactical models of healthcare units, and at level 3 are strategic models.

Seck & Honig (2012) introduced a multi-perspective modeling approach that can be applied to any domain (and not in healthcare M&S only). Therefore, perspectives are not specifically identified, but a generic conceptual framework is proposed and formalized by adding to the DEVS systems specification hierarchy, a top layer to represent multi-perspective models.

An integration approach, very similar to ours, is proposed in (Jeffers, 2014), and though not formalized. The common denominator chosen to specify models is System Dynamics.

A key issue in developing multi-perspective models is the validity of the bridging components, i.e., the way parameters of a model are disaggregated using outputs of other models. Authors in (Duboz et al., 2003) first asserted the need of awareness for such a legitimacy issue. If a parameter in one component varies in time according to the output of another component, then the status of the parameter change, becoming a new type of state variable. The assumptions made in the former component should stay valid. For instance, if the former component is a differential equation, by varying one of its parameter at runtime, we should insure that the numerical integration scheme we use to compute the equation is still stable.

The SES extension to integrate abstraction hierarchies and time granularity, as proposed in (Santucci et al., 2016), provides a convenient ontological framework that will allow us to

extend the multi-perspective modeling approach beyond healthcare systems, towards a more generic framework.

6. Conclusion

We have proposed a framework for multi-perspective modelling and holistic simulation of healthcare systems. Furthermore, we have developed an integrative approach for the interactions between models of different perspectives through dynamic update of models output-to-parameter integration during concurrent simulations. Such an approach provides multiple levels of explanation for the same system, while offering, at the same time, an integrated view of the whole. The novelty of our approach is that notable components of the healthcare system are modeled as autonomous systems that can influence and be influenced by their environments. The resulting global model can be coupled with a holistic experimental frame to derive results that couldn't be accurately addressed in any of the perspective taken alone.

Furthermore, we have connected this framework to process-based M&S results previously established, to allow domain experts bring their knowledge at the conceptual modeling level, while model transformation can turn the abstractions described into their DEVS counterparts. Our future direction is to expand on the coordination dimension, towards M&S for value-based learning healthcare systems.

Acknowledgement

Through this article, the authors want to pay tribute to Norbert Giambiasi, not in the sense that he directly mentored or supervised this work, but because of the impact that his scientific legacy can (and will surely continue to) have in our community, through its various facets, as illustrated in this research effort.

References

- (Ahmed & Alkhamis, 2009) Ahmed M.A., Alkhamis T.M. 2009. Simulation optimization for an emergency department healthcare unit in Kuwait. *European Journal of Operational Research* 198(3):936-942.
- (Allen, 1976) Allen P.M. 1976. Evolution, Population Dynamics, and Stability. *Proceedings of the National Academy of Sciences- USA*, 73:665-68.
- (Augusto & Xie, 2014) Augusto V., Xie X. 2013. Modelling and Simulation Framework for Health Care Systems. *IEEE Transactions on Systems, Man and Cybernetics, Part A: Systems and Humans*, Institute of Electrical and Electronics Engineers 44 (1):30-46.
- (Barjis, 2011) Barjis J. 2011. Healthcare simulation and its potential areas and future trends. *SCS M&S Magazine* 2(5) :1-6.
- (Bazoun et al., 2014) Bazoun H., Bouanan Y., Zacharewicz G., Ducq Y., Boye H. 2014. Business process simulation: transformation of BPMN 2.0 to DEVS models (WIP). In *Proceedings of the Symposium on Theory of Modeling & Simulation – DEVS Integrative M&S Symposium*, Society for Computer Simulation International, page 20.

(Bisset et al., 2012) Bisset K.R., Eubank S., Marathe M.V. 2012. High Performance Informatics for Pandemic Preparedness. Proceedings of the 2012 Winter Simulation Conference, IEEE.

(Bohk et al., 2009) Bohk C., Ewald R., Uhrmacher A., Probabilistic Population Projection with James II, In Proceedings of the 2009 Winter Simulation Conference, pp. 2008-2019.

(Bountourelis et al., 2011) Bountourelis T., Ulukus M.Y., Kharoufeh J.P., Nabors S.G. 2011. The modeling, analysis, and management of intensive care units. In Handbook of Healthcare Operations Management. Springer New York, pp. 153-182.

(Brailsford et al., 2003) Brailsford S., Schmidt B. 2003. Towards incorporating human behaviour in models of healthcare systems: An approach using discrete event simulation. European Journal of Operational Research 150(1):19-31.

(Brailsford et al., 2011) Brailsford S., Silverman E., Rossiter S., Bijak J., Shaw R., Viana J., Noble J., Efstathiou S., Vlachantoni A. 2011. Complex Systems Modeling for Supply and Demand in Health and Social care. Proceedings of the 2011 Winter Simulation Conference, pp. 1125-1136.

(Brailsford, 2007) Brailsford S.C. 2007. Advances and challenges in healthcare simulation modeling: tutorial. Proceedings of the 39th Winter Simulation Conference. IEEE Press, pp. 1436-1448.

(Carr & Roberts, 2010) Carr S., Roberts S. 2010. Planning for Infectious Disease Outbreaks: A Geographic Disease Spread, Clinic Location, and Resource Allocation Simulation. Proceedings of the 2010 Winter Simulation Conference. IEEE, pp. 2171-2184.

(Cetinkaya et al., 2012) Cetinkaya D., Verbraeck A., Seck M.D. 2012. Model transformation from BPMN to DEVS in the MDD4MS framework. In Proceedings of the 2012 Symposium on Theory of Modeling and Simulation – DEVS Integrative M&S Symposium. Society for Computer Simulation International, page 28.

(Charfeddine & Montreuil, 2010) Charfeddine M., Montreuil B. Integrated Agent-Oriented Modeling and Simulation of Population and Healthcare Delivery Network: Application to COPD Chronic Disease in a Canadian Region. In Proceedings of the 2010 Winter Simulation Conference, pp. 2327- 2339.

(Cote, 1999) Cote M.J. 1999. Patient flow and resource utilization in an outpatient clinic. Socio-Economic Planning Sciences 33(3):231-245.

(Davis et al., 2013) Davis A., Mehrotra S., Friedewald J., Ladner D. 2013. Characteristics of a Simulation Model of the National Kidney Transplantation System. In Proceedings of the 2013 Winter Simulation Conference: Simulation: Making Decisions in a Complex World. IEEE Press, pp. 2320-2329.

(Dibble, 2010) Dibble C. 2010. Effective Real-Time Allocation of Pandemic Interventions. In Simulation Conference (WSC), Proceedings of the 2010 Winter Simulation Conference. IEEE, pp. 2211-2220

(Duboz et al., 2003) Duboz R., Ramat E., Preux P. 2003. Scale Transfer Modeling: Using Emergent Computation for Coupling Ordinary Differential Equation System with a Reactive Agent Model. Systems Analysis Modelling Simulation 43(6):793–814.

(Ferranti & Freitas Filho, 2011) Ferranti J., Freitas Filho P. 2011. Dynamic Mortality Simulation Model Incorporating Risk Indicators for Cardiovascular Diseases, In Proceedings of the 2011 Winter Simulation Conference, pp. 1263-1274.

(Findlay & Grant, 2011) Findlay M., Grant H. 2011. An Application of Discrete-Event Simulation to an Outpatient Healthcare Clinic with Batch Arrivals. In Proceedings of the 2011 Winter Simulation Conference (WSC). IEEE, pp. 1166-1177.

- (Fletcher et al., 2009) Fletcher A., Worthington D. 2009. Generic simulation modelling of A&E patient flows through the whole hospital. *Operations Research Applies to Health Services (ORAHs)*.
- (Giambiasi et al., 2008) Giambiasi N., Escude B., Ghosh S., (2000). G-DEVS A Generalized Discrete Event Specification for Accurate Modeling of Dynamic Systems. *SCS Transactions Volume 17, 3*, p.120-134.
- (Gunal & Pidd, 2010) Günal M.M., Pidd M. 2010. Discrete event simulation for performance modelling in health care: a review of the literature. *Journal of Simulation* 4(1):42-51.
- (Harper, 2002) Harper P.R. 2002. A framework for operational modelling of hospital resources. *Health care management science*, 5(3), 165-173, 2002.
- (Hollingsworth, 1995) Hollingsworth D. 1995. The Workflow Reference Model. *Workflow Management Coalition Spec., WfMC-TC-1003*.
- (Jeffers, 2014) Jeffers R.F. 2014. A Model of Population Movement, Disease Epidemic, and Communication for Health Security Investment. In United States. National Nuclear Security Administration.
- (Jouault et al., 2008) Jouault Frédéric, Freddy Allilaire, Jean Bézivin, Ivan Kurtev, ATL: A model transformation tool, *Science of Computer Programming*, Volume 72, Issues 1–2, 1 June 2008, Pages 31-39, ISSN 0167-6423
- (Kasaie et al., 2013) Kasaie P., Dowdy D.W., Kelton W.D. 2013. An Agent-Based Simulation of a Tuberculosis Epidemic: Understanding the Timing of Transmission. In *Proceedings of the 2013 Winter Simulation Conference: Simulation: Making Decisions in a Complex World*. IEEE Press, pp. 2227-2238.
- (Khurma et al., 2013) Khurma N., Salamati F., Pasek, Z.J. 2013. Simulation of Patient Discharge Process and its Improvement. In *2013 Winter Simulations Conference*. IEEE, pp. 2452-2462.
- (Kuhl, 2012) Kuhl M.E. 2012. A Simulation Study of Patient Flow for Day of Surgery Admission. In *Proceedings of the 2012 Winter Simulation Conference*. IEEE, pp. 1-7.
- (Leslie, 1945) Leslie P.H. 1945. On the Use of Matrices in Certain Population Mathematics. *Biometrika* 33(3):183-212.
- (Macal et al., 2012) Macal C.M., David M.Z., Dukic V.M., Lauderdale D.S., North M.J., Shumm P., Collier N., Daum R.S., Wegener D.T., Evans J.A., Wilder J.R. 2012. Modeling the Spread of Community-Associated MRSA. *Proceedings of the 2012 Winter Simulation Conference*. IEEE, 12p.
- (Marmor et al., 2011) Marmor Y.N., Rohleder T.R., Huschka T., Cook D., Thompson J., Clinic M. 2011. A Simulation Tool to Support Recovery Bed Planning for Surgical Patients. In *Proceedings of the 2011 Winter Simulation Conference (WSC)*, IEEE, pp. 1333-1339.
- (Mittal et al., 2007) Mittal S., Risco-Martin J-L., Zeigler B.P. DEVS-Based Simulation Web Services for Net-Centric T&E. In *Proceedings of the 2007 summer computer simulation conference*. Society for Computer Simulation International, pages 357–366.
- (Muzy & Zeigler 2017) Muzy A., Zeigler B.P. 2014. Specification of Dynamic Structure Discrete Event Systems Using Single Point Encapsulated Functions. *International Journal of Modeling, Simulation and Scientific Computing* 5(3): 1450012 (20 pages).
- (Okhmatovskaia et al., 2012) Okhmatovskaia A., Buckeridge D., Shaban-Nejad A., Sutcliffe A., Fins P., Kopec J., Wolfson M. 2012. SIMPHO: an Ontology for Simulation Modeling of Population Health, In *Proceedings of the 2012 Winter Simulation Conference*, pp. 1-12.
- (OMG, 2011) Object Management Group, Business Process Management Initiative et al. 2011. Business Process Model and Notation (BPMN) version 2.0. Available on: <http://www.omg.org/spec/BPMN/2.0>.

(Onggo, 2012) Onggo B.S. 2012. Simulation Modeling in the Social Care Sector: A literature Review. In Proceedings of the 2012 Winter Simulation Conference, pp. 739-750.

(Ozcan et al., 2011) Ozcan Y.A., Tãnfani E., Testi A. 2011. A simulation-based modeling framework to deal with clinical pathways. In Proceedings of the Winter Simulation Conference, pp. 1190-1201.

(Partridge et al., 2013) Partridge C., Mitchell A., De Cesare S. 2013. Guidelines for developing ontological architectures in modelling and simulation. In *Ontology, Epistemology, and Teleology for Modeling and Simulation*. Springer, Berlin Heidelberg, pages 27–57.

(Puri et al., 2011) Puri C.A., Gomadam K., Jain P., Yeh P.Z., Verma K. 2011. Multiple ontologies in healthcare information technology: Motivations and recommendation for ontology mapping and alignment. In ICBO.

(Ramirez-Nafarrate & Gutierrez-Garcia, 2013) Ramirez-Nafarrate A., Gutierrez-Garcia J.O. 2013. An Agent-Based Simulation Framework to analyze the Prevalence of Child Obesity. In Proceedings of the 2013 Winter Simulation Conference, pp. 2330-2339.

(Redding et al., 2014) Redding S., Conrey E., Porter K., Paulson J., Hughes K., Redding M. 2014. Pathways Community Care Coordination in Low Birth Weight Prevention. *Maternal and Child Health Journal* 18(6):1-8.

(Roberts, 2011) Roberts S.D. 2011. Tutorial on the simulation of healthcare systems. In Proceedings of the Winter Simulation Conference, pp. 1408-1419.

(Santucci et al., 2016) Santucci J.F., Capocchi L., Zeigler B.P. 2016. System Entity Structure Extension to Integrate Abstraction Hierarchies and Time Granularity into DEVS Modeling and Simulation. *Simulation* 92 (8): 747-769.

(Seck & Honig, 2012) Seck M.D., Honig H.J. 2012. Multi-perspective Modelling of Complex Phenomena. *Computational and Mathematical Organization Theory* 18:128–144.

(Sheppard, 1985) Sheppard E. 1985. Urban system population dynamics: incorporating nonlinearities. *Geographical analysis Columbus* 17(1):47-73.

(Sikdar & Karmeshu, 1982) Sikdar P.K., Karmeshu P.K. 1982. On Population Growth of Cities in a Region: A Stochastic Nonlinear Model. *Environment and Planning A* 14:585-90.

(Silver et al., 2007) Silver G.A., Hassan O.A.H., Miller J.A. 2007. From Domain Ontologies to Modeling Ontologies to Executable Simulation Models. In 2007 Winter Simulation Conference, IEEE, pp. 1108-1117.

(Sobolev et al., 2008) Sobolev B., Harel D., Vasilakis C., Levy A. 2008. Using the Statecharts Paradigm for Simulation of Patient Flow in Surgical Care. *Health Care Management Science* 11(1):79-86.

(Van der Aalst & Van Hee, 2002) Van Der Aalst WMP, Van Hee K.M. 2002. *Workflow Management: Models, Methods, and Systems*. The MIT Press, Cambridge, Massachusetts.

(Verma & Gupta, 2013) Verma S., Gupta A. 2013. Improving Services in Outdoor Patient Departments by Focusing on Process Parameters: A Simulation Approach. In Proceedings of the 2013 Winter Simulation Conference, pp. 2250-2261.

(Viana et al., 2012) Viana J., Rossiter S., Channon A.R., Brailsford S.C., Lotery A.J. 2012. A Multi-Paradigm, Whole System View of Health and Social Care for Age-Related Macular Degeneration. *Proceedings of the 2012 Winter Simulation Conference*. IEEE.

(Weng et al. 2011) Weng S.J., Tsai B.S., Wang L.M., Chang C.Y., Gotcher D. 2011. Using simulation and data envelopment analysis in optimal healthcare efficiency allocations. In Proceedings of the Winter Simulation Conference, pp. 1295-1305.

(WMC, 1999) Workflow Management Coalition. 1999. Terminology & Glossary. WfMC-TC-1011, 3.0, Feb.

- (Zacharewicz et al., 2008) Zacharewicz G., Frydman C.S., Giambiasi N. 2008. G-DEVS/HLA environment for distributed simulations of workflows. *Simulation* 84:197–213.
- (Zeigler et al., 2012) Zeigler B.P., Carter E., Seo C., Russell C.K., Leath B.A. 2012. Methodology and modeling environment for simulating national health care. In *Autumn Simulation Multi-Conference (AutumnSim'12)*, pp. 30-46.
- (Zeigler et al., 2014) Zeigler B.P., Carter E.L., Redding S.A., Leath B.A. 2014. Pathways Community HUB: A Model for Coordination of Community Health Care. *Population Health Management* 17(4):199-201.
- (Zeigler, 1976) Zeigler B.P. 1976. *Theory of modeling and simulation*. John Wiley & Sons. Inc., New York, NY.
- (Zeigler, 1984) Zeigler B.P. 1984. *Multifaceted Modelling and Discrete Event Simulation*. Academic Press Inc., London.
- (Zeigler, 2017) Zeigler B.P. 2017. How Can Modeling and Simulation Help Engineering of System of Systems? *Computational Frameworks: Systems, Models and Applications* (Traoré Ed.). ISTE Press – Elsevier. ISBN: 9781785482564. Chapter 1.
- (Zeigler & Hammond, 2007) Zeigler B.P., Hammonds P.E. 2007. *Modeling and Simulation-based Data Engineering: Introducing Pragmatics into Ontologies for Netcentric Information Exchange*. Academic Press Professional.
- (Zeigler & Sarjoughian, 2017) Zeigler B.P., Sarjoughian H.S. 2017. *Guide to Modeling and Simulation of Systems of Systems*, Second Edition, Springer, Berlin, Germany.
- (Zeshan & Mohamad, 2012) Zeshan F., Mohamad R. 2012. Medical ontology in the dynamic healthcare environment. *Procedia Computer Science* 10:340–348.
- (Zulkepli et al., 2012) Zulkepli J., Eldabi T., Mustafee N. 2012. Hybrid Simulation for Modelling Large Systems: An example of Integrated Care Model. *Proceedings of the 2012 Winter Simulation Conference, IEEE*.

Appendix

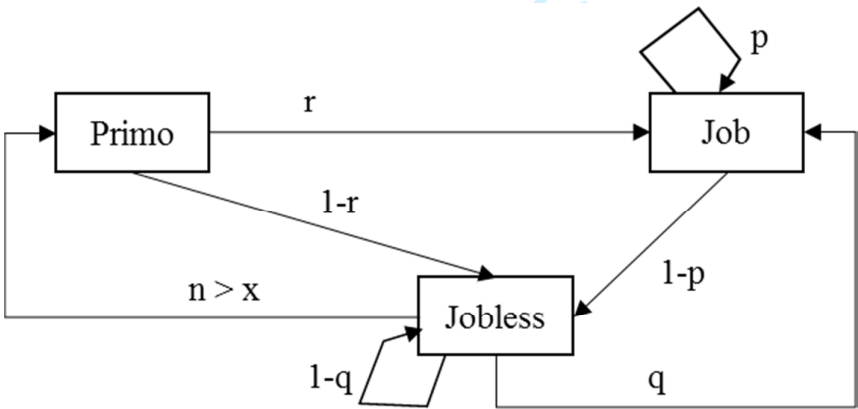
A1. Ebola spreading model (compartmental model)

$$\begin{aligned}\frac{dS}{dt} &= -\beta SI - \alpha SD \\ \frac{dE}{dt} &= \beta SI + \alpha SD - \sigma E \\ \frac{dI}{dt} &= \sigma E - \gamma I \\ \frac{dR}{dt} &= (1-f)\gamma I \\ \frac{dD}{dt} &= f\gamma I\end{aligned}$$

where

- S is the number of susceptible individuals in the population
- E the number of exposed individuals (susceptible individuals become exposed before being infected)
- I is the number of infectious individuals I
- R is the number of recovered individuals
- D is the number of dead individuals
- β is the transmission rate with infected individuals
- α is the transmission rate with dead individuals
- σ is the incubation rate
- γ is the “recovery or death” rate
- f is the case fatality rate

A2. Daily worker model (Agent-based model)



- r is the probability for a primo entering (i.e., a daily worker in a new working area) to get a job daily
- p is the probability for a worker to keep the same job for the next day
- q is the probability for a jobless to find a new job
- x is the number of days after which a jobless will relocate
- it takes 3 days to a primo entering to establish and understand how the local market works

A3. Interstate migrations model (Cellular Automata)

$$n_i(t+1) = g_i n_i(t) + \sum_{j \neq i} (\alpha_i - \alpha_j) |n_i - n_j| e^{-\tau d_{ij}}$$

where

- $n_i(t)$ is the population of state i at time t
- g_i is the net growth rate (i.e., birth – death +/- migrations from/towards outside the country) of state i
- α_i is the relative attractivity of state i (i.e., the GDP per capita of state i over the GDP per capita of the country)
- d_{ij} is the distance between capital cities of states i and j
- τ is a constant positive number

A4. Hospital beds allocation model (Forrester System Dynamics model)

